

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of

Conf. No.: 4395

Timo HEINRICH et al.

Group Art Unit: 1625

Serial No.: 10/590,912

Examiner: Celia C. Chang

Filed: February 14th, 2005

For: INDOL-PIPERIDINE

DECLARATION UNDER 37 C.F.R. '1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Joachim Leibrock, being duly warned declare that:

I am a citizen of the Federal Republic of Germany, residing at Pfungstadt, Germany.

I am a biochemist and molecular biologist by training and experience.

The degree of Ph.D. (Dr. rer. nat.) was bestowed on me by the University of München (Munich), Germany.

Since January the 1st, 1991 I have been employed as a biochemist in the CNS department of Merck KGaA, Darmstadt, Germany.

Since January the 1st, 2003 I have been employed as a biochemist in the Diabetes Research department of Merck KGaA, Darmstadt, Germany and since December the 1st, 2008, I have been employed as a biochemist in the Immunopharmacology department of Merck-Serono, Darmstadt, Germany.

I am author or co-author of papers and patents in the fields of biochemistry, molecular biology and pharmacology.

The following pharmacological tests of some typical compounds within the pharmacological field of serial no. 10/5590,912 have been conducted by me or under my supervision:

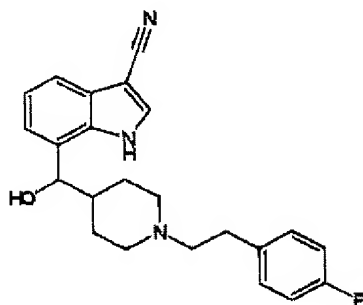
Description of the assay method:

3H-Ketanserin inhibition assay (5-HT_{2A} receptor) internal code: SOP 2831

The assay was performed as already described (Klockow et al., 1986). For the human recombinant 5-HT_{2A} receptor, a stable CHO-K1 cell line expressing this receptor (Euroscreen ES-313-M) was utilized, using about 15 µg of membrane protein per assay. Alternatively, rat cortical membranes (1 mg protein per assay, Klockow et al., 1986) were used. The assay contained (final volume 1 ml): 0.5 nM 3H-ketanserin, 50 mM Tris-HCl, pH 7.4 and 10 µM methysergide for nonspecific binding. Incubations were carried out at 37 °C for 15 min.

Literature:

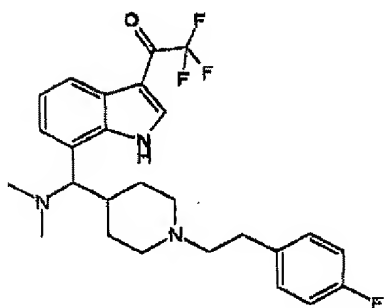
Klockow M, Greiner HE, Haase A, Schmitges C-J, Seyfried C. Studies on the receptor profile of bisoprolol. Drug Res 1986; 36: 197-200.

**I1**

EMD 515127

MSC 1830014

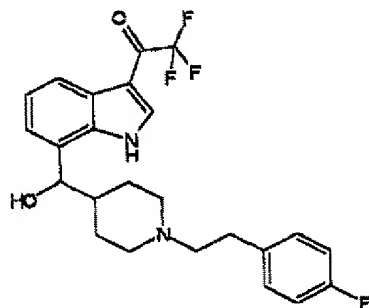
SOP 2831: 3 nM

**I2**

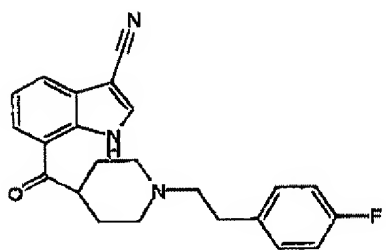
EMD 515126

MSC 1830013

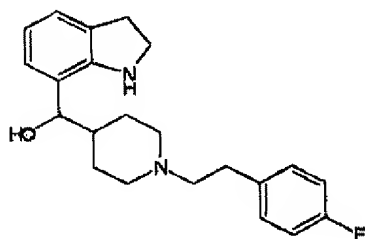
2831: 330 nM



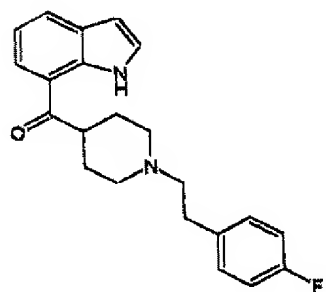
13
EMD 515125
MSC 1830018
2831: 31 nM



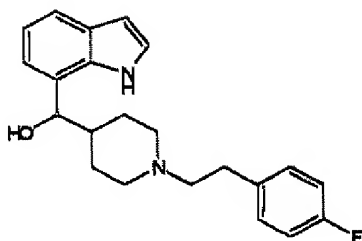
14
EMD 514692
MSC 1829237
2831: 140 nM



15
EMD 513343
MSC 1827783
2831: 27 nM



16
EMD 513247
MSC 1826963
2831: 120 nM



17

EMD 513162


MSC 1826208

2831: 2.2 nM

Compounds claimed in US Patent Application No. 10/590,912 show remarkable activity on inhibition of 5HT_{2A} receptor. Compounds having 5HT_{2A} receptor inhibiting activity can be used for treating disorders like Parkinson's Disease has been published in Fernandez et al. Clin Neuropharmacol. 2004 Jan-Feb; 27(1):4-5.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

April, 8th, 2010
Date


Joachim Leibrock